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## ORIGINAL ARTICLE

# An efficient and simple synthesis of $\alpha$ -amino phosphonates as ‘drug like’ molecules catalyzed by silica-supported perchloric acid ( $\text{HClO}_4\text{-SiO}_2$ )

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Heterogeneous catalyst;  
Multi-component;  
Trialkyl phosphite

**Abstract** An efficient and direct protocol is described for the preparation of  $\alpha$ -amino phosphonates derivatives by employing a multi-component, one-pot condensation reaction of aldehyde, amine and trialkyl phosphite in the presence of silica-supported perchloric acid (3 mol%) under solvent-free conditions. The thermal solvent-free green procedure offers advantages such as shorter reaction time, simple work-up, high yield, recovery and reusability of catalyst.

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## 1. Introduction

The synthesis and use of phosphonate-containing molecules as an important class of active compounds, have received increased attention during the last two decades (Engle and Cohen, 2003; Savignac and Iorga, 2003). In this relation, the utilities of  $\alpha$ -amino phosphonates as HIV protease (Peyman

et al., 1992, 1994), anti-thrombotic agents (Meyer and Barlett, 1998), enzyme inhibitors (Allen et al., 1989), antibiotics (Atherton et al., 1986), peptid mimics (Kafarski and Leczak, 1991), herbicides, fungicides, insecticides (Maier and Spörri, 1990), as well as important role for antibody generation (Smith III et al., 1994), are well documented. Because of their pharmacological and biological importance, many procedures for the synthesis of  $\alpha$ -amino phosphonates have been developed. Among the numerous reported methods, the nucleophilic addition reaction of phosphites with imines is one of the most convenient of these methods, and usually catalyzed by base (Pudovik, 1952), Bronsted (Petrov et al., 1974), or Lewis acids such as  $\text{BF}_3\text{-OEt}_2$  (Ha and Nam, 1992),  $\text{SnCl}_4$  (Laschate and Kunz, 1992). However, these methods are not devoid of their limitation as many imines are hygroscopic and are not sufficiently stable for isolation. In the other hands, these reactions cannot be proceeded in a one-pot reaction involving a carbonyl compound, an amine and a trialkyl phosphite, because the amines and water exist during imine formation can decompose or deactivate the Lewis acid (Yokomatsu et al., 1994).

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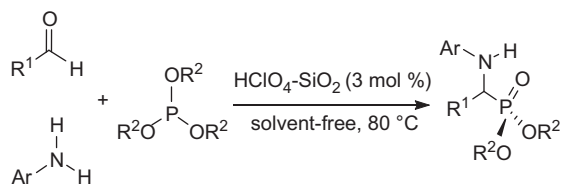
To overcome some of these problems, recently one-pot three-component synthesis of  $\alpha$ -amino phosphonates has been developed. This conversion has been carried out by employing catalysts including lanthanide triflate (Qian and Huang, 1998), indium(III) chloride (Ranu et al., 1999), lithium perchlorate (Saidi and Azizi, 2002), magnesium perchlorate (Bhagat and Chakraborti, 2007),  $\text{TaCl}_5\text{-SiO}_2$  (Chandrasekhar et al., 2001),  $\text{PhNMe}_3\text{Cl}$  (Heydari and Arefi, 2007),  $\text{TiO}_2$  (Hosseini-Sarvari, 2008), sulfamic acid (Mitrageotri et al., 2008),  $\text{In}(\text{OTf})_3$  (Ghosh et al., 2004),  $\text{CF}_3\text{CO}_2\text{H}$  (Akiyama et al., 2003), Amberlite-IR 120 (Bhattacharya and Rana, 2008),  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  (Heydari et al., 2007), Amberlyst-15 (Tajbakhsh et al., 2008), oxalic acid (Vahdat et al., 2008), trifluoroethanol (Heydari et al., 2009),  $\text{Na}_2\text{CaP}_2\text{O}_7$  (Elmakssoudi et al., 2005), [emim]Br (Yavari and Hajinasiri, 2009). However, many of these methods have drawbacks: for instance, long reaction time, environmental pollution caused by means of organic solvents, and expensive catalyst. Therefore, there is a need to develop a facile one-pot synthesis of  $\alpha$ -amino phosphonates without these problems. The use of solid acidic catalysts supported on silica has attracted much attention in organic synthesis due to their advantages such as, reusability, inexpensiveness, ease of preparation and handling, nontoxicity, operational simplicity and ease of isolation from the reaction mixture. Silica-supported perchloric acid ( $\text{HClO}_4\text{-SiO}_2$ ) is well known as an efficient heterogeneous catalyst for various chemical reactions (Chakraborti and Gulhane, 2003; Kumar et al., 2007, 2006; Khan et al., 2006; Bigdeli et al., 2007; Das et al., 2007; Kantevari et al., 2007; Shaterian et al., 2007). In continuation of our research works in the synthesis of  $\alpha$ -amino phosphonates (Maghsoodlou et al., 2009, 2010), herein, we employed the silica-supported perchloric acid as an efficient and reusable heterogeneous acid catalyst for one-pot three-component synthesis of  $\alpha$ -amino phosphonates under solvent-free conditions at 80 °C (Scheme 1).

## 2. Experimental

Melting points and IR spectra of all compounds were measured on an Electrothermal 9100 apparatus and a Shimadzu IR-460 spectrometer, respectively. The  $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{31}\text{P}$  NMR spectra were obtained on BRUKER DRX-250 AVANCE instruments with  $\text{CDCl}_3$  as a solvent. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on Agilent Technology (HP) spectrometer operating at an ionization potential of 70 eV. All reagents and solvents obtained from Fluka and Merck were used without further purification.

### 2.1. General experimental procedure

The aldehyde (1 mmol), amine (1.2 mmol) and  $\text{HClO}_4\text{-SiO}_2$  (60 mg, 3 mol%) were stirred for a few minutes. Then trialkyl



**Scheme 1** Synthesis of  $\alpha$ -amino phosphonates.

phosphite (1 mmol) was added. The mixture was stirred at 80 °C in oil bath for the appropriate time (see Table 2). After completion of the reaction (followed by TLC), the reaction mixture was cooled and  $\text{CH}_2\text{Cl}_2$  (20 mL) was added. The catalyst was separated by simple filtration and the filtrate was washed with  $\text{H}_2\text{O}$  ( $3 \times 10$  mL). The organic layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$  and was evaporated. The crude product was purified by silica gel column chromatography with *n*-hexane/ethyl acetate (7:3) as eluent to provide pure  $\alpha$ -amino phosphonates. Spectral data for new products are represented below:

### 2.2. Compound 16 (Table 2, entry 16)

Yellow solid, mp 131–133 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 250 MHz)  $\delta$ : 3.45 (3H, d,  $^3J_{\text{PH}} = 10.5$  Hz, P–OCH<sub>3</sub>), 3.67 (3H, s, OCH<sub>3</sub>), 3.75 (3H, s, OCH<sub>3</sub>), 3.80 (3H, d,  $^3J_{\text{PH}} = 10.7$  Hz, P–OCH<sub>3</sub>), 3.89 (3H, s, OCH<sub>3</sub>), 4.18 (1H, br, NH), 5.25 (1H, d,  $^2J_{\text{PH}} = 24.0$  Hz, CHP), 6.44–6.70 (6H, m, Ar), 7.37 (1H, m, Ar);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 62.5 MHz)  $\delta$ : 48.12 (d,  $^1J_{\text{PC}} = 156.3$  Hz), 53.68 (d,  $^2J_{\text{PC}} = 6.9$  Hz), 53.84 (d,  $^2J_{\text{PC}} = 6.9$  Hz), 55.27, 55.61, 55.79, 98.52, 104.90 (d,  $J = 2.5$  Hz), 114.67, 115.05, 116.40, 128.97 (d,  $J = 5.0$  Hz), 140.02 (d,  $J = 15.6$  Hz), 152.61, 158.18 (d,  $J = 6.9$  Hz), 160.51;  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ , 101 MHz)  $\delta$ : 26.41; IR (KBr)  $\nu$ : 3320 (NH), 1235 (P=O), 1060, 1039 (P–O–Me); MS  $m/z$  (%): 381 ( $\text{M}^+$ , 14), 272 (100), 259 (10), 257 (11), 149 (88), 123 (53), 121 (69), 109 (6), 92 (10), 79 (18), 77 (17). Anal. Calcd. for  $\text{C}_{18}\text{H}_{24}\text{NO}_6\text{P}$ : C, 56.69; H, 6.34; N, 3.67; Found: C, 56.83; H, 6.49; N, 3.75.

### 2.3. Compound 17 (Table 2, entry 17)

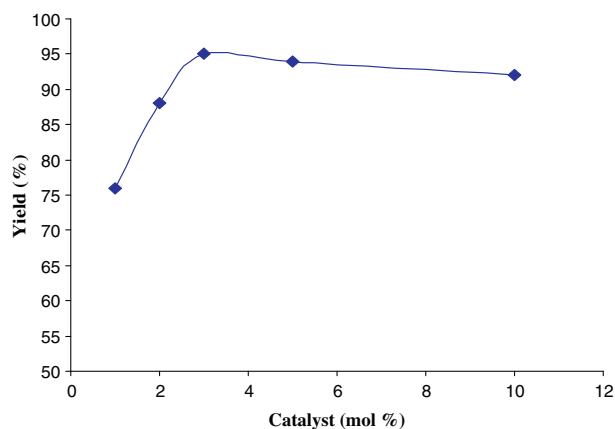
White solid, mp 84–85 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 250 MHz)  $\delta$ : 3.54 (3H, d,  $^3J_{\text{PH}} = 10.5$  Hz, P–OCH<sub>3</sub>), 3.83 (3H, d,  $^3J_{\text{PH}} = 10.5$  Hz, P–OCH<sub>3</sub>), 3.85 (3H, s, OCH<sub>3</sub>), 3.98 (3H, s, OCH<sub>3</sub>), 4.63 (1H, br, NH), 5.43 (1H, d,  $^2J_{\text{PH}} = 24.0$  Hz, CHP), 6.56–7.11 (7H, m, Ar);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 62.5 MHz)  $\delta$ : 47.74 (d,  $^1J_{\text{PC}} = 156.4$  Hz), 53.68 (d,  $^2J_{\text{PC}} = 6.9$  Hz), 53.90 (d,  $^2J_{\text{PC}} = 6.9$  Hz), 55.65, 60.93, 112.16 (d,  $J = 2.4$  Hz), 113.34 (d,  $J = 2.6$  Hz), 114.51 (d,  $J = 18.4$  Hz), 118.02 (d,  $J = 6.9$  Hz), 119.70 (d,  $J = 4.0$  Hz), 124.31 (d,  $J = 2.6$  Hz), 124.53 (d,  $J = 3.4$  Hz), 129.27, 134.42 (dd,  $J = 14.7$  Hz,  $J = 11.3$  Hz), 147.03 (d,  $J = 7.3$  Hz), 151.90 (d,  $^1J_{\text{FC}} = 273.8$  Hz), 152.33 (d,  $J = 1.7$  Hz);  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ , 101 MHz)  $\delta$ : 25.17; IR (KBr)  $\nu$ : 3316 (NH), 1240 (P=O), 1052, 1030 (P–O–Me); MS  $m/z$  (%): 369 ( $\text{M}^+$ , 6), 260 (100), 245 (10), 135 (16), 123 (13), 122 (11), 111 (21), 109 (10), 95 (8), 79 (10). Anal. Calcd. for  $\text{C}_{17}\text{H}_{21}\text{FNO}_5\text{P}$ : C, 55.29; H, 5.73; N, 3.79. Found: C, 55.41; H, 5.70; N 3.76.

### 2.4. Compound 18 (Table 2, entry 18)

White solid, mp 94–96 °C.  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$ : 3.62 (3H, d,  $^3J_{\text{PH}} = 10.8$  Hz, P–OCH<sub>3</sub>), 3.86 (3H, d,  $^3J_{\text{PH}} = 10.9$  Hz, P–OCH<sub>3</sub>), 4.62 (1H, br, NH), 5.80 (1H, d,  $^2J_{\text{PH}} = 28.8$  Hz, CHP), 6.49–6.54 (2H, m, Ar), 7.14–7.37 (5H, m, Ar);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 62.5 MHz)  $\delta$ : 52.74 (d,  $^1J_{\text{PC}} = 156.9$  Hz), 53.63 (d,  $^2J_{\text{PC}} = 6.9$  Hz), 53.93 (d,  $^2J_{\text{PC}} = 7.5$  Hz), 110.79, 115.26, 128.55 (d,  $J = 1.3$  Hz), 129.66 (d,  $J = 3.1$  Hz), 130.58 (d,  $J = 2.5$  Hz), 130.68, 132.06, 134.75 (d,  $J = 5.0$  Hz), 136.66 (d,  $J = 6.9$  Hz), 144.57 (d,  $J = 15.6$

**Table 1** Optimization amount of silica supported perchloric acid for the reaction between benzaldehyde, aniline and trimethyl phosphite under solvent-free conditions at 80 °C.

Entry	Catalyst (mol%)	Time (min)	Yield (%) <sup>a</sup>
1	1	100	76
2	2	85	88
3	3	65	95
4	5	55	94
5	10	35	92

<sup>a</sup> Yields refer to the pure isolated products.**Figure 1** The reaction between benzaldehyde, aniline and Trimethyl phosphite in the presence of different mol% of  $\text{HClO}_4\text{-SiO}_2$ .

Hz);  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ , 101 MHz)  $\delta$ : 22.54; IR (KBr)  $\nu$ : 3324 (NH), 1255 (P=O), 1061, 1017 (P–O–Me); MS  $m/z$  (%): 439 ( $\text{M}^+$ , 8), 332 (80), 330 (100), 328 (86), 294 (9), 249 (8), 184 (14), 157 (13), 155 (13), 109 (6), 76 (18). Anal. Calcd. for  $\text{C}_{15}\text{H}_{15}\text{BrCl}_2\text{NO}_3\text{P}$ : C, 41.03; H, 3.44; N, 3.19. Found: C, 41.20; H, 3.49; N, 3.28.

### 2.5. Compound 19 (Table 2, entry 19)

White solid, mp 136–137 °C.  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$ : 3.48 (3H, d,  $^3J_{\text{PH}} = 10.5$  Hz, P–OCH<sub>3</sub>), 3.82 (3H, d,  $^3J_{\text{PH}} = 10.7$  Hz, P–OCH<sub>3</sub>), 3.86 (3H, s, OCH<sub>3</sub>), 3.96 (3H, s, OCH<sub>3</sub>), 4.26 (1H, br, NH), 5.35 (1H, d,  $^2J_{\text{PH}} = 24.0$  Hz, CHP), 6.54 (2H, d,  $J = 8.8$  Hz, Ar), 6.82–7.08 (3H, m, Ar), 7.17 (2H, d,  $J = 8.8$  Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 62.5 MHz)  $\delta$ : 48.06 (d,  $^1J_{\text{PC}} = 155.6$  Hz), 53.80 (d,  $^2J_{\text{PC}} = 6.9$  Hz), 53.85 (d,  $^2J_{\text{PC}} = 6.9$  Hz), 55.67, 60.94, 110.40, 112.18 (d,  $J = 2.5$  Hz), 115.48, 119.64 (d,  $J = 4.4$  Hz), 124.34 (d,  $J = 2.5$  Hz), 129.00, 131.92, 144.88 (d,  $J = 15.0$  Hz), 146.95, 152.33;  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ , 101 MHz)  $\delta$ : 25.42; IR (KBr)  $\nu$ : 3317 (NH), 1267 (P=O), 1054, 1018 (P–O–Me); MS  $m/z$  (%): 431 ( $\text{M} + 2$ , 6), 429 ( $\text{M}^+$ , 7), 322 (100), 320 (89), 241 (6), 154 (8), 135 (13), 121 (9), 109 (9), 91 (6), 79 (8). Anal. Calcd. for  $\text{C}_{17}\text{H}_{21}\text{BrNO}_5\text{P}$ : C, 47.46; H, 4.92; N, 3.26. Found: C, 47.41; H, 4.97; N 3.24.

### 2.6. Compound 20 (Table 2, entry 20)

Brownish solid, mp 112–114 °C.  $^1\text{H}$  NMR (250 MHz,  $\text{CDCl}_3$ )  $\delta$ : 3.46 (3H, d,  $^3J_{\text{PH}} = 10.5$  Hz, P–OCH<sub>3</sub>), 3.70 (3H, s, OCH<sub>3</sub>), 3.80 (3H, d,  $^3J_{\text{PH}} = 10.6$  Hz, P–OCH<sub>3</sub>), 3.88 (3H, s, OCH<sub>3</sub>),

**Table 2** Preparation of  $\alpha$ -amino phosphonates.

Entry	R1	Ar	R2	Time (min)	Yield (%) <sup>a</sup>	Ref. <sup>b</sup>
1	Ph	Ph	Me	65	95	Bhagat and Chakraborti, 2007
2	Ph	Ph	Et	100	93	Qian and Huang, 1998
3	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Ph	Me	40	94	Heydari and Arefi, 2007
4	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Ph	Et	55	95	Hosseini-Sarvari, 2008
5	3-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Ph	Et	46	91	Bhattacharya and Rana, 2008
6	4-OH-C <sub>6</sub> H <sub>4</sub>	Ph	Me	90	89	Bhagat and Chakraborti, 2007
7	4-F-C <sub>6</sub> H <sub>4</sub>	Ph	Et	75	94	Bhattacharya and Rana, 2008
8	2-Cl-C <sub>6</sub> H <sub>4</sub>	Ph	Me	55	94	Vahdat et al., 2008
9	2-Cl-C <sub>6</sub> H <sub>4</sub>	Ph	Et	90	93	Hosseini-Sarvari, 2008
10	3-Cl-C <sub>6</sub> H <sub>4</sub>	Ph	Et	100	90	Hosseini-Sarvari, 2008
11	4-Cl-C <sub>6</sub> H <sub>4</sub>	Ph	Me	60	94	Heydari and Arefi, 2007
12	4-Me-C <sub>6</sub> H <sub>4</sub>	Ph	Et	180	81	Bhattacharya and Rana, 2008
13	4-NMe <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Ph	Me	80	92	Bhagat and Chakraborti, 2007
14	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub>	Ph	Me	120	73	Tajbakhsh et al., 2008
15	CH <sub>3</sub> CHCH <sub>3</sub>	Ph	Me	120	71	Tajbakhsh et al., 2008
16	2,4-di-OMe-C <sub>6</sub> H <sub>3</sub>	4-OMe-C <sub>6</sub> H <sub>4</sub>	Me	70	97	–
17	2,3-di-OMe-C <sub>6</sub> H <sub>3</sub>	2-F-C <sub>6</sub> H <sub>4</sub>	Me	70	96	–
18	2,6-di-Cl-C <sub>6</sub> H <sub>3</sub>	4-Br-C <sub>6</sub> H <sub>4</sub>	Me	45	98	–
19	2,3-di-OMe-C <sub>6</sub> H <sub>3</sub>	4-Br-C <sub>6</sub> H <sub>4</sub>	Me	70	95	–
20	2,5-di-OMe-C <sub>6</sub> H <sub>3</sub>	4-Cl-C <sub>6</sub> H <sub>4</sub>	Me	75	95	–
21	3-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	3-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Et	120	93	Ghosh et al., 2004
22	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Me	85	90	Bhagat and Chakraborti, 2007
23	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	Et	120	89	Bhagat and Chakraborti, 2007

<sup>a</sup> Yields refer to the pure isolated products.<sup>b</sup> All known products have been reported previously in the literature and were characterized by comparison of IR and NMR spectra with authentic samples. All new compounds characterized by melting point, IR, NMR ( $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{31}\text{P}$ ), Mass spectroscopies and Elemental analyses.

**Table 3** Recyclability of the catalyst for the reaction between benzaldehyde, aniline and trimethyl phosphite in the presence of  $\text{HClO}_4\text{-SiO}_2$  (3 mol%).

Run No.	Yield (%) <sup>a</sup>
1	95
2	94
3	91
4	88
5	83

<sup>a</sup> Yields refer to the pure isolated recovered catalyst.

4.25 (1H, br, NH), 5.32 (1H, d,  $^2J_{\text{PH}} = 24.8$  Hz, CHP), 6.51–7.04 (7H, m, Ar);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 62.5 MHz)  $\delta$ : 47.93 (d,  $^1J_{\text{PC}} = 156.9$  Hz), 53.70 (d,  $^2J_{\text{PC}} = 6.9$  Hz), 53.87 (d,  $^2J_{\text{PC}} = 6.9$  Hz), 55.63, 56.37, 111.78, 113.80, 113.96, 114.79, 123.04, 124.74, 128.99, 144.47, 144.71, 151.44;  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ , 101 MHz)  $\delta$ : 25.47; IR (KBr)  $\nu$ : 3310 (NH), 1252 (P=O), 1040, 1024 (P–O–Me); MS  $m/z$  (%): 385 ( $\text{M}^+$ , 9), 276 (100), 261 (37), 246 (30), 149 (21), 140 (18), 111 (16), 109 (8), 79 (11). Anal. Calcd. for  $\text{C}_{17}\text{H}_{21}\text{ClINO}_5\text{P}$ : C, 52.93; H, 5.49; N, 3.63. Found: C, 53.04; H, 5.45; N 3.71.

### 3. Results and discussion

Silica-supported perchloric acid was prepared according to the literature procedure (Chakraborti and Gulhane, 2003). In order to find out the optimum quantity of silica-supported perchloric acid, a reaction between benzaldehyde, aniline and trimethyl phosphite was carried out under solvent-free conditions using different quantities of  $\text{HClO}_4\text{-SiO}_2$  (Table 1 and Fig. 1). As seen in Fig. 1, silica-supported perchloric acid with 3 mol% gives excellent yield in 65 min at 80 °C.

Hence, a series of  $\alpha$ -amino phosphonates were prepared in high to excellent yields from the reaction between aldehyde (1 mmol), amine (1.2 mmol) and trialkyl phosphites (1 mmol) in the presence of silica-supported perchloric acid (3 mol%). The results are summarized in Table 2.

As can be seen from Table 2, each benzaldehyde containing electron-deficient or electron-releasing groups reacts efficiently with aniline for generation of the corresponding  $\alpha$ -amino phosphonates (Table 2, entries 1–13). Also the reactions between substituted aniline, substituted benzaldehyde and trimethyl/triethyl phosphite led to the desired  $\alpha$ -amino phosphonate in good yield (Table 2, entries 16–23). In addition, this method is effective even with aliphatic aldehydes, which normally produce low yields due to their intrinsic lower reactivity (Table 2, entries 14 and 15). On the basis of experimental results, the rate of all the reactions in the presence of trimethyl phosphite was increased in comparison with triethyl phosphite under constant conditions. The wide applicability of the present method is evident from the fact that it is tolerant towards various functional groups including alkoxy, halides and nitro groups. We have also prepared five new analogues of these compounds in excellent yields (Table 2, entries 16–20). These new compounds characterized by melting point, IR, NMR ( $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{31}\text{P}$ ), Mass spectroscopies and Elemental analyses.

The reusability of the catalysts is an important benefit in present method and makes it useful for commercial applica-

tions. Thus, the recyclability of the catalyst was checked for the reaction between benzaldehyde, aniline and trimethyl phosphite in the presence of  $\text{HClO}_4\text{-SiO}_2$  (3 mol%). The separated catalyst can be reused after washing with MeOH and drying at 100 °C. The results indicate that the catalyst can be used five times without any loss of its activity (Table 3).

### 4. Conclusion

Thus, we have demonstrated that silica supported perchloric acid is an efficient and green catalyst for the synthesis of  $\alpha$ -amino phosphonates.  $\alpha$ -amino phosphonate derivatives were prepared via a one-pot three-component reaction between aryaldehyde, amine and trialkyl phosphite in the presence of catalytic silica-supported perchloric acid in solvent-free conditions. The thermal solvent-free green procedure offer advantages such as shorter reaction time, high yields, environmentally benign, simple work-up, cost effective recovery and the reusability of catalyst for a few times without a significant change in its activity.

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